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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/957,045 10/24/97 DALUGE S PB1517US3

HM12/0324

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EXAMINER

BERCH, M

ART UNIT

PAPER NUMBER

1524

16

DATE MAILED: 03/24/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Best Available Copy

Advisory ActionApplication No.
08/957,045

Applicant(s)

Daluge

Examiner

Mark L. Berch

Group Art Unit

1624**THE PERIOD FOR RESPONSE:** [check only a) or b)]

- a) ☐ expires _____ months from the mailing date of the final rejection.
- b) ☐ expires either three months from the mailing date of the final rejection, or on the mailing date of this Advisory Action, whichever is later. In no event, however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

- ☒ Appellant's Brief is due two months from the date of the Notice of Appeal filed on Mar 17, 2000 (or within any period for response set forth above, whichever is later). See 37 CFR 1.191(d) and 37 CFR 1.192(a).

Applicant's response to the final rejection, filed on Mar 17, 2000 has been considered with the following effect, but is **NOT** deemed to place the application in condition for allowance:

- ☒ The proposed amendment(s):

☐ will be entered upon filing of a Notice of Appeal and an Appeal Brief.

- ☒ will not be entered because:

- ☒ they raise new issues that would require further consideration and/or search. (See note below).
- ☐ they raise the issue of new matter. (See note below).
- ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.
- ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: See memo

- ☐ Applicant's response has overcome the following rejection(s):

- ☐ Newly proposed or amended claims _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claims.
- ☐ The affidavit, exhibit or request for reconsideration has been considered but does **NOT** place the application in condition for allowance because:
- ☐ The affidavit or exhibit will **NOT** be considered because it is not directed **SOLELY** to issues which were newly raised by the Examiner in the final rejection.
- ☒ For purposes of Appeal, the status of the claims is as follows (see attached written explanation, if any):
- Claims allowed: _____
- Claims objected to: _____
- Claims rejected: 9 and 18-22

- ☐ The proposed drawing correction filed on _____ ☐ has ☐ has not been approved by the Examiner.
- ☐ Note the attached Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☐ Other

MARK L. BERCH
PRIMARY EXAMINER
ART UNIT 1624

Art Unit: 1624

DETAILED ACTION

The amendment filed 3/17/00 under 37 CFR 1.116 in reply to the final rejection has been considered but is not deemed to place the application in condition for allowance and will not be entered because: The proposed amendment raises new issues that would require further consideration and/or search.

The revised R³ definition has expanded the choice after the third semicolon so that it now appears to completely encompass the material which appears after the second semicolon. It is thus not clear why this latter material is present at all.

Further, the explanation of what constitutes a "glycosidic bond" only makes matters worse. The arrow that applicants have labeled as being to a "glycosidic bond" in fact points to an ordinary single bond. Moreover, its application to the current claims is unclear. The claims are drawn to preparation of purine derivatives, but there is no purine in this structure. Further, the bond depicted is not the bond which attaches the R³ as required by the claim language, but rather appears to be a bond internally present in the R³ moiety. Moreover, the remarks do not appear to be aware of this, referring to R³ choices which are bound by N, i.e. which are substituted amines. See first full sentence on page 5 of the remarks. But that is impossible. R³ cannot be bound by a N, unless that N is part of a heterocyclic ring as set forth in the last R³ choice. Thus, for example, the moiety depicted on page 5, if bound by the N is not a permitted choice for R³. Note previous discussion of this point in the Final

Art Unit: 1624

Rejection over EP 413,544 in view of newly cited Norbeck, Vince, Borthwick or Shealy.

Beyond that, assuming that what the claim is trying to say is that R^3 cannot be a moiety derived from a sugar, the claim would still be indefinite. There is no single generally accepted definition of what does and does not constitute a sugar and hence what moiety would qualify as an aglycone piece. The material depicted at the bottom of page 4 has three OH groups. Would it still be an aglycone if one, two or three OH groups were missing, or if an additional OH or hydroxymethyl group were present, or if the two OH groups attached to the ring were attached to the same carbon instead of adjacent carbons? If the ring size were 4, 6, 7 or 10 instead of 5? If the ring had 1 sulfur, nitrogen or carbon instead of one oxygen, or if it had 2 oxygens instead of just one? If the ring were unsaturated, bridged or fused to another ring? If the ring had other substituents such as amino, halo, acetoxy or a heterocycle? Are acyclic versions included in the definition of the aglycone?

The traverse of the rejection over Daluge '697 in view of Vince '224 or Daluge '671, further in view of Norbeck, Vince '607, Borthwick or Shealy is unpersuasive. Applicants point to the low yield of Shealy, example 1, and problems with the Vince and Borthwick, etc. But these are not the primary references. These are solely a secondary references, cited only to show that the use of aqueous acid is conventional for orthoformate cyclizations (Norbeck, Vince '607, Borthwick or Shealy) or to show removing the N-2 protecting group early (as is done by applicant) rather than later.

Art Unit: 1624

Thus, while the remarks state, "disadvantages of the '607 process are...", the claims are not rejected over the '607 process itself.

With regard to the essential difference, that is, removing the protecting group early versus late, applicants must actually demonstrate a difference, rather than make unsubstantiated assertions like, "deprotection before ring closure causes the compound to fall apart." The essential difference is that applicants remove the protecting group earlier rather than later. A direct side by side comparison must be made to show that unexpected effects arise from this, because the variation of removing the protecting group later is shown by both Vince '224 and Daluge '671. It is not considered hindsight because that procedure was already shown in those two references (note that they are from different research groups). Especially, example 4 of '671 provides excellent motivation of a cyclization being successfully done with the 2-position being unprotected.

The traverse of the EP 413,544 in view of Norbeck, Vince, Borthwick or Shealy rejection is also unpersuasive. Applicants statement that $O(CH_2)_3OR_5$ is outside the current claims is not agreed with. The group in the reference is a protected OH, as was pointed out in the paper of 1/28/99. That is, $O(CH_2)_3OR_5$ is a protected OH.

With regard to better yields, etc, applicants must present a side by side comparison using the same substituent. Applicants point to example 8 of their application, but that does not use the same substituent as is seen in the prior art. Applicants point out that the reference does not use aqueous acid but that is explicitly

Art Unit: 1624

taught by the secondary references. The reference is not asserted to be an anticipation, only that it renders the claims obvious. Applicants present no justification for calling this a matter of hindsight. Four references show that the use of aqueous acid is conventional for orthoformate cyclizations. One of ordinary skill in the art of organic synthesis would thus be aware of such an expedient, and the fine results obtained in the secondary references would motivate their use.

The traverse of the rejection over Norbeck, Vince, Borthwick or Shealy, in view of EP 413,544 or Daluge '697 is also unpersuasive. Essentially the same issues arise here as in the other two discussions above.

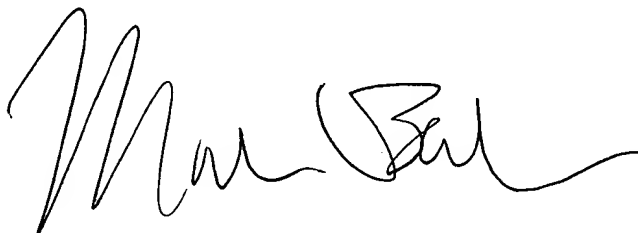
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Mark L. Berch whose telephone number is 703-308-4718.

Mark L. Berch

Primary Examiner

Group 1610 - Art Unit 1624

March 23, 2000

A handwritten signature in black ink, appearing to read 'Mark L. Berch', with a stylized, cursive script.